



Increases in Hemoglobin Recovery After IV Iron Therapy Mediate Improvements in Ambulatory Capacity in Critical Illness Survivors: A Secondary Analysis of the PABST-BR Clinical Trial

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BACKGROUND

Anemia is common after surgery and critical illness and impacts negatively multidimensional recovery metrics and overall quality of life.

The PABST-BR clinical trial tested an anemia prevention and treatment bundle –including a single dose of IV iron– versus standard cares in 100 critically ill adults of which 65% were post-surgical patients.

The intervention bundle led to significant improvements in hemoglobin recovery through 3 months post-hospitalization. Effect estimates also suggested possible benefits across physical, cognitive, and mental health functional domains.

This secondary analysis examines how changes in hemoglobin and iron-status markers at 1 month may contribute to improvements and clinical outcomes.

METHODS

Mediation analyses were employed to evaluate how changes in 1-month post-hospitalization hemoglobin concentrations and iron studies (ferritin, transferrin saturation [Tsat], and soluble transferrin receptor [sTfR]) from baseline enrollment values impact patient functional status at 1-month post-hospitalization.

Physical function was assessed with the 6-minute walk distance (6MWD) and FACIT-Fatigue survey.

Cognition was assessed with the Montreal Cognitive Assessment (MoCA) and mental health was assessed with the hospital anxiety and depression scale (HADS).

Quality of life was assessed with the EQ-5D.

Linear and generalized mixed-effects models were used to assess outcomes using proportional odds models for scores outcomes and logistic models for yes-or-no outcomes with adjustment for baseline laboratory values, age, and sex.

A linear combination of treatment and time point by treatment interaction term estimated the treatment effect at 1-month follow-up. Results with a p-value <0.05 were considered statistically significant.

RESULTS

- **Changes in hemoglobin concentrations from baseline to 1-month post-hospitalization were associated with improved ambulatory capacity.**
- **Each 1 g/dL increase in hemoglobin was accompanied by a mean 108 ft increase in 6MWD (p = 0.012).**
- **There were no other statistically significant relationships between hemoglobin change and functional outcomes.**
- **Changes in Tsat values were inversely associated with cognition scores, with a decrease of 0.04 in total cognition assessment score per each 1% increase in Tsat (p = 0.027).**
- **There were no other statistically significant mediation effects by iron markers on patient functional status.**

Outcome	Effect per increase in laboratory value	Estimate	Standard Error	P-value
6MWD (ft)	Hemoglobin (per 1 g/dL)	108	43	*0.012
	Ferritin (per 10 ng/mL)	0.05	1.5	0.96
	Tsat (per 1%)	10.5	7.6	0.16
	sTfR (per 1 unit increase)	67.5	38	0.076
FACIT-Fatigue	Hemoglobin (per 1 g/dL)	0.196	0.129	0.13
	Ferritin (per 10 ng/mL)	-0.0015	0.0053	0.77
	Tsat (per 1%)	-0.0104	0.015	0.49
	sTfR (per 1 unit increase)	0.1882	0.1544	0.22
MoCA	Hemoglobin (per 1 g/dL)	0.154	0.135	0.25
	Ferritin (per 10 ng/mL)	-0.0048	0.0055	0.38
	Tsat (per 1%)	-0.036	0.0163	*0.027
	sTfR (per 1 unit increase)	0.1911	0.1579	0.22
HADS-Anxiety	Hemoglobin (per 1 g/dL)	-0.032	0.13	0.80
	Ferritin (per 10 ng/mL)	-0.0037	0.0055	0.50
	Tsat (per 1%)	0.020	0.0157	0.18
	sTfR (per 1 unit increase)	-0.1492	0.1555	0.33
HADS-Depression	Hemoglobin (per 1 g/dL)	-0.0506	0.128	0.69
	Ferritin (per 10 ng/mL)	0.0031	0.0053	0.56
	Tsat (per 1%)	0.0236	0.0156	0.13
	sTfR (per 1 unit increase)	-0.2793	0.1570	0.075
EQ-5D	Hemoglobin (per 1 g/dL)	0.088	0.129	0.49
	Ferritin (per 10 ng/mL)	-0.0030	0.0053	0.57
	Tsat (per 1%)	-0.0188	0.0156	0.22
	sTfR (per 1 unit increase)	0.2689	0.1570	0.086

TABLE 1: Mediation Effects of Hemoglobin and Iron Markers on Patient Functional Status.

DISCUSSION

- Increasing hemoglobin concentrations after critical illness is associated with meaningful improvements in ambulatory capacity.
- IV iron therapy may enhance post-hospital recovery of physical function primarily by raising hemoglobin levels rather than by restoring serum iron availability.
- A small inverse association was observed between transferrin saturation (Tsat) and cognitive scores, though this is likely not clinically meaningful and lacks a clear physiological explanation.
- Larger clinical trials are needed to clarify these relationships and to better understand the mechanisms through which anemia treatment may support patient recovery.

CONCLUSIONS

- Hemoglobin improvement at 1 month emerged as the only laboratory change linked to better physical performance, reinforcing its importance in post-critical illness recovery.
- Other markers of iron status –ferritin, sTfR, sTfR-FI– did not meaningfully predict functional outcomes at this early recovery time point.
- Our results highlight the need for larger studies to elucidate how anemia management strategies may translate into sustained functional benefits post-hospitalization following critical illness.

REFERENCES

Practical Anemia Bundle and Hemoglobin Recovery in Critical Illness. JAMA Network Open. 2025;8(3):e252353. doi;10.1001/jamanetworkopen.2025.2353.